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<b>(54) Title:</b> ANTIMICROBIAL CONTACT LENS CASE  <b>(57) Abstract</b>  The present invention relates to an antimicrobial contact lens case and an ophthalmic solution container that are comprised of an antimicrobial polymeric resin and have antimicrobial surfaces, but which do not contaminate the lens or solution with antimicrobial agent. The present invention provides a novel antimicrobial contact lens container which is adapted to hold one or more contact lenses and ophthalmic solution. The contact lens container is made from a polymeric material containing zeolite which has ion-exchanged thereon silver ions in an amount from about 0.1 to 5 wt.% of the zeolite and ammonium ions in an amount from about 0.5 to 15 wt.% of the zeolite. The zeolite is present in an amount from about 0.5 to 5 wt. % of the polymeric material. The contact lens container of the invention does not leach ions from the polymeric material into the ophthalmic solution in a substantially antimicrobial amount.		

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## ANTIMICROBIAL CONTACT LENS CASE

### 5     FIELD OF THE INVENTION

The present invention relates to an antimicrobial contact lens case and an ophthalmic solution container that contain an antimicrobial polymeric resin and have antimicrobial surfaces, but which do not contaminate the lens or solution with antimicrobial agent.

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### BACKGROUND OF THE INVENTION

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Contact lenses are often exposed to microorganisms, which can result in infections developing after the lenses are used. Conventional contact lenses should be periodically disinfected by the user to prevent infection or other deleterious effects on ocular health associated with contact lens wear. There are several conventional systems and methods aimed at preventing microbial contamination of contact lenses.

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The majority of commercial ophthalmic solutions, including those used for the care of contact lenses, are packaged in dispensing bottles molded from a thermoplastic or thermosetting resin. Such solutions include saline solutions, cleaning solutions which incorporate a cleaning agent, and conditioning solutions. Since these solutions usually come into direct contact with contact lenses or the eye, it is important that the solutions do not become contaminated with microorganisms, such as infectious bacteria. The usual method used to avoid bacterial contamination of the solution involves packaging the solution under sterile conditions and designing the container to minimize the likelihood of contamination from handling. Additionally, the solution can incorporate a preservative to inhibit growth of microorganisms.

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Microbial contamination of contact lens cases is a significant problem. Contaminated contact lens cases are implicated in microbial keratitis. A disinfected contact lens placed in a contaminated contact lens case may itself become contaminated. This negates the beneficial effects of the lens disinfection. Contact lens cases are continually

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exposed to environmental contaminants, as well as to contact lenses which may become contaminated from handling or use, and as a consequence, the cases often provide a substratum for biofilm which is nutritive and protective of microorganisms.

5 Most eye care systems designed to combat microbial growth are directed to making the ophthalmic solution antimicrobial. It would be beneficial, however, to have a contact lens case which has antimicrobial properties, to prevent the growth of microbes thereon and consequential contamination of lenses.

Contact lens cases designed for storage of contact lenses or for a care regimen of the lenses are generally constructed of a thermoplastic or thermosetting resin. When a  
10 contact lens is placed in a contact lens cell of the case, it is immersed in ophthalmic solution. The usual method employed to inhibit microbial growth on the contact lens case cells is to avoid contamination of the case to the extent possible, to cap the cell during use, and to rinse the case between uses. Microbial growth may also be inhibited by the solution placed in the contact lens cell.

15 It is known that silver ions can be incorporated in ophthalmic solutions to inhibit bacterial or microbial growth. For example, Schweisfurth et al. (Contactologia, Vol. 7 D (1985), pages 144-147) disclose antibacterial properties of silver containing solutions used for storage and disinfection of contact lenses. Additionally, a sodium silver chloride complex (SoluSept, Similasan AG, Switzerland) has been used as a preservative for ophthalmic  
20 solutions. In each case, the silver imparts antimicrobial properties to the ophthalmic solution.

U.S. Pat. No. 5,320,843 issued to Raheja et al. (Raheja '843) provides a method for improving the antibacterial efficacy of an ophthalmic solution used in the care of contact lenses. The method uses an article molded from a plastic resin including an aluminosilicate carrier, such as zeolite, retaining antibacterial metal ions. Ophthalmic  
25 solution is placed in contact with the article. To render the solution antimicrobial, the zeolite releases metal ions into the ophthalmic solution in contact with the case.

The contact lens case of Raheja '843 incorporates antimicrobial zeolite such as that prepared according to U.S. Pat. No. 4,525,410 issued to Hagiwara *et al.* (Hagiwara '410). The zeolite incorporated therein retains silver ions in an amount from 0.001 to 10% by weight of anhydrous zeolite, or copper ions or zinc ions in an amount from 0.01 to 25% by weight of  
30 anhydrous zeolite. In accordance with Raheja '843, it is preferred if the zeolite carrier described therein is incorporated in the resin at 0.01 to 30% by weight of the resin, with 0.5 to

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10% being more preferred. The antimicrobial zeolite incorporated in the contact lens case taught by Raheja '843 provides release of antibacterial metal ions into the ophthalmic solution to render the solution antibacterial.

5 It is often undesirable, when using conventional ophthalmic disinfecting solutions to have an additional agent, i.e., silver, migrating from the container into the solution. Antimicrobial solution comprising silver ions can interact in unpredictable ways with the ingredients in the solution, and could inactivate the solution or adversely react with it. Such ingredients include phosphate-buffered saline and NaCl. For example, the phosphate in PBS could precipitate with silver resulting in a change in pH of the ophthalmic solution. In addition, silver may react with chloride ions from NaCl to form silver chloride, 10 which can cause serious irritation in the eye of a user of the solution. Furthermore, marketing of a case that leaches substantial amounts of silver into an ophthalmic solution requires regulatory approval as a drug in some jurisdictions.

15 Nevertheless, it would be advantageous for a contact lens case or container to have antimicrobial properties that prevent growth of bacteria thereon, but which does not leach substantial amounts of antimicrobial agent into ophthalmic solution placed in the case or container.

#### SUMMARY OF THE INVENTION

20 The present invention provides a novel antimicrobial contact lens container which is adapted to hold one or more contact lenses and ophthalmic solution. The contact lens container is made from a polymeric material containing zeolite which has ion-exchanged thereon silver ions in an amount from about 0.1 to 5 wt.% of the zeolite and ammonium ions in an amount from about 0.5 to 15 wt.% of the zeolite. The zeolite is present in an amount 25 from about 0.5 to 5 wt. % of the polymeric material. The contact lens container of the invention does not leach silver ions from the polymeric material into the ophthalmic solution in a substantially antimicrobial amount.

30 It has been determined that such a container avoids contamination of ophthalmic solution with antimicrobial agent leached from zeolite contained in the polymer from which the container is formed. For example, the container does not release silver in a "spike" on initial contact with the solution, as occurs with other types of zeolite. Instead, the silver is released at a slow rate, and in amounts that are small enough to avoid imparting

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antimicrobial properties to the solution. The rate of leaching of silver ions into a solution in contact with a container of the invention is controllable by the amount of silver ion-exchanged with zeolite and the manner in which the zeolite is incorporated into the container. Furthermore, adjusting the amount of ammonium or zinc ions will alter the rate of release of silver.

Accordingly, the invention further provides a novel container or bottle for use in dispensing ophthalmic solutions, which container has the aforementioned antimicrobial properties. Thus, in describing herein the properties and composition of a contact lens case of the invention, the same is applicable to a container for dispensing ophthalmic solutions.

The present lens case has novel antimicrobial properties that reduce microbial contamination of the case, and consequently, of the lenses which may be stored in such case. By making the contact lens case itself antimicrobial, the present invention provides a means of preventing microbial contamination and growth on the case but allows all types of ophthalmic solutions to be employed in the container. Furthermore, substantial antimicrobial properties are not imparted to the solution, nor are the characteristics of ophthalmic solutions altered. In addition, regulatory approval for sale of such a case may not normally be required.

The antimicrobial characteristics of the container of invention reduce the likelihood of contamination, since ophthalmic solution above may not kill, or even reduce microbial growth adhered to the case and protected by biofilm. As noted above, if a conventional case becomes contaminated, a biofilm may form on the surface of the case due to colonization of the contaminating microorganisms. Such a biofilm provides means for bacteria to survive even when later subjected to an antimicrobial or other preserved solution since the biofilm "protects" microorganisms from contacting the solution. The present invention provides a method of inhibiting the formation of such a biofilm on the surfaces of the contact lens case without the use of a contacting ophthalmic solution.

The antimicrobial component of the case does not migrate into or through a liquid medium to provide the desired antimicrobial properties. Instead, the antimicrobial components are substantially non-leachable from the present contact lens case into the liquid media. Furthermore, no substantial "spike" effect is observed whereby a large amount of silver ion is initially released when the zeolite in the container is contacted with an aqueous solution. Thus, the antimicrobial components of the invention remain associated with the

lens case and are effective for relatively long periods of time, even indefinitely.

#### BRIEF DESCRIPTION OF THE DRAWINGS

5       **FIGURE 1** is a top perspective view of one embodiment of the contact lens case of the invention.

**FIGURE 2** is a cross-sectional view taken along line 2-2 of Figure 1 showing one embodiment of the contact lens case of the invention which shows antimicrobial zeolite dispersed throughout the polymeric material comprising the contact lens case.

10       **FIGURE 3** is a cross-sectional view taken along line 3-3 of Figure 1 showing one embodiment of the contact lens case of the invention which shows antimicrobial zeolite dispersed throughout the polymeric material comprising the contact lens case.

**FIGURE 4** is a cross-sectional view of a mold for making one embodiment of the contact lens case of the invention which shows antimicrobial zeolite on the external surface of the mold.

15       **FIGURE 5** is a cross-sectional view taken along line 3-3 of Figure 1 showing one embodiment of the contact lens case of the invention which shows antimicrobial zeolite dispersed in the polymeric material comprising the contact lens case and on the surfaces of the case which contact ophthalmic solution.

20       **FIGURE 6** is a top perspective view of one embodiment of the contact lens case of the invention.

**FIGURE 7** is a cross-sectional view taken along line 7-7 of one embodiment of the contact lense case of the invention which shows antimicrobial zeolite dispersed in the polymeric material comprising the contact lens case.

25       **FIGURE 8** is a cross-sectional view of a mold for making one embodiment of a contact lens case of the invention showing antimicrobial zeolite on the external surface of the mold.

**FIGURE 9** is a cross-sectional view taken along line 7-7 of one embodiment of the contact lens case of the invention showing antimicrobial zeolite on the surfaces of the case which contact ophthalmic solution.

30       **FIGURE 10** is a top perspective view of one embodiment of a contact lens solution container of the invention.

**FIGURE 11** is a cross-sectional view taken along line 11-11 of a contact lens

solution container showing antimicrobial zeolite dispersed throughout the polymeric material comprising the container.

FIGURE 12 is a cross-sectional view taken along line 11-11 of a contact lens solution container showing antimicrobial zeolite on the surfaces of the container which contact ophthalmic solution.

FIGURES 13 is a graph showing the concentration of silver ions detected in ophthalmic saline solution as mV over time and quantified over a 6.5 hour period.

#### DETAILED DESCRIPTION OF THE INVENTION

All patents, patent publications, and literature references cited in this specification are hereby incorporated by reference in their entirety.

As used herein, antimicrobial, antibacterial, microbicidal, bactericidal, antibiotic, microbicidally, bactericidally, and the like, shall include an amount of compound at least equal to the minimum inhibitory concentration (MIC), discussed *infra.*, for a particular microbe, and may be used interchangeably.

As used herein, the term "active", when used to describe an ingredient of a contact lens case or container of the present invention, shall be limited to the antimicrobial compounds of the invention.

As used herein, the term "effective amount" is used synonymously with "sufficient amount", both terms referring to the amount of active ingredient in a container of the invention required to achieve the antimicrobial properties thereof.

As used herein, the terms "about" or "approximately" shall mean within 20 percent, preferably within 10 percent, and more preferably within 5 percent of a given value or range.

As used herein "non-leachable" into ophthalmic solution in a substantially antimicrobial amount shall mean that silver is not released from the article which contains it, into an aqueous contacting media over a period of twenty-four hours in an amount sufficient to impart to the media the antimicrobial property or characteristic otherwise desired of that media. For example, antimicrobial zeolite is substantially non-leachable in this manner if it imparts antimicrobial properties to a contact lens case of the invention, but imparts no substantial antimicrobial activity to the contacting aqueous media after twenty-four hours of exposure.



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In its broadest aspect, the present invention is directed to contact lens care containers, such as an ophthalmic solution bottle, or a contact lens case, which comprise at least one container section, preferably two container sections, sized and adapted to define a space which holds a lens, preferably a contact lens, when the lens is not in use in the eye. The container section of the contact lens case is made at least partially, and preferably substantially of a material comprising a polymeric material and an antimicrobial component which is substantially non-leachable, as defined above, under normal use conditions. The zeolite described herein can be readily incorporated in a plastic resin, e.g., by kneading, and the resultant mixture can be processed into containers by conventional molding techniques. Preferably, the container section is structured so that the contact lens held in the container section contacts the material making up the container section.

In a particularly useful embodiment, the lens case is structured so that liquid, for example, a saline solution, can enter therein and contact the lens being held in the space defined by the container section. The antimicrobial component may be present primarily, or even substantially at or near the external surface of the container section, e.g., as a coating, and preferably at an external surface which contacts the lens being held in the space defined by the container section. Alternatively, the antimicrobial component may be substantially uniformly distributed throughout the container section.

The following patent publications disclose antibacterial zeolites retaining silver ions, and various polymer articles having antibacterial properties which contain the zeolite: U.S. Pat. No. 4,525,410; U.S. Pat. No. 4,775,585; U.S. Pat. No. 4,906,464; U.S. Pat. No. 4,911,898; U.S. Pat. No. 4,911,899; U.S. Pat. No. 4,938,955; U.S. Pat. No. 4,938,958; U.S. Pat. No. 5,003,638; U.S. Pat. No. 5,064,599; U.S. Pat. No. 5,085,416; abstract of Japan 02/080,442; and abstract of Japan 02/125,717.

Silver ions are believed to exert their antimicrobial effects by disrupting respiration and electron transport systems upon absorption into bacterial or fungal cells. Antimicrobial silver ions are particularly safe due to the fact that they are not substantially absorbed into the body. Thus, use of silver containing compositions allows for an exceptionally safe, non-toxic formulation useful in contact lens cases and lens care product containers. Thus, the invention provides a means for preventing growth of microbes by killing organisms that would otherwise contaminate a contact lens container lacking the antimicrobial properties of the invention. More preferably, the invention provides a means

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for killing or preventing the growth of bacteria, which may include, but are not necessarily limited to *S. aureus*, *S. epidermidis*, *C. albicans*, *P. vulgaris*, *S. mutans*, and *P. aeruginosa*.

In a preferred embodiment, antimicrobial ceramic particles are formulated in a contact lens case or contact lens care container of the invention to provide antimicrobial activity that is long lasting. Furthermore, it has been determined that such formulation used in the present invention is able to adequately kill microorganisms, including microorganisms which are exposed to a contact lens while in or out of the eye, over a prolonged period of time.

The antimicrobial zeolite for use in the contact lens case of the invention, can be prepared according to conventional methods known in the art. Zeolite particles preferably have a particle diameter size from about 0.2 to 40  $\mu\text{m}$ , more preferably between about 0.5 to 5  $\mu\text{m}$ . They include the antimicrobial zeolites disclosed, for example, in U.S. Patent Nos. 4,938,955 issued to Niira *et al.* Zeolites disclosed in 4,911,898 issued to Hagiwara *et al.* that do not contain ion-enhanced ammonium have been found to permit metal ions retained thereon to quickly leach in large quantities into ophthalmic solution. This particular zeolite is therefore not suitable for the present invention. Zeolite retaining metal ions prepared in accordance with Niira '955 lack this property and can be used advantageously to form a contact lens case of the invention.

Ion release rate experiments show that a contact lens case or container of the invention has the capability of effecting substantial antimicrobial action over long periods of time without substantial leaching of antimicrobial particles into a solution in contact therewith. The release rate of antimicrobial metal ions from zeolite in a typical container of the invention is less than about 100 parts per billion (ppb) per day, which release rate is substantially constant over time, i.e., there is no "spike" effect. Therefore, the contact lens case or container is incapable of making a solution in the container antimicrobial.

Natural zeolites and synthetic zeolites can be used to make the antimicrobial zeolites of the present invention. "Zeolite" is an aluminosilicate having a three dimensional skeletal structure that is represented by the formula:  $\text{XM}_{2n}\text{O}-\text{Al}_2\text{O}_3-\text{YSiO}_2-\text{ZH}_2\text{O}$ . M represents an ion-exchangeable ion, generally a monovalent or divalent metal ion,  $n$  represents the atomic valency of the (metal) ion, X and Y represent coefficients of metal oxide and silica respectively, and Z represents the number of water of crystallization. Examples of such zeolites include A-type zeolites, X-type zeolites, Y-type zeolites, T-type

zeolites, high-silica zeolites, sodalite, mordenite, analcite, clinoptilolite, chabazite and erionite. The present invention is not restricted to any specific types of zeolite carriers.

The ion-exchange capacities of these zeolites are as follows: A-type zeolite = 7 meq/g; X-type zeolite = 6.4 meq/g; Y-type zeolite = 5 meq/g; T-type zeolite = 3.4 meq/g; sodalite = 11.5 meq/g; mordenite = 2.6 meq/g; analcite = 5 meq/g; clinoptilolite = 2.6 meq/g; chabazite = 5 meq/g; and erionite = 3.8 meq/g. These ion-exchange capacities are sufficient for the zeolites to undergo ion-exchange with ammonium and antimicrobial metal ions.

The specific surface area of preferred zeolite particles is at least about 150 m<sup>2</sup>/g (anhydrous zeolite as standard) and the SiO<sub>2</sub>/Al<sub>2</sub>O<sub>3</sub> mol ratio in the zeolite composition is preferably less than 14, more preferably less than 11.

The antimicrobial silver ions used in the zeolites of the invention can be retained on the zeolite particles through an ion-exchange reaction. Antimicrobial metal ions which are merely adsorbed or attached without an ion-exchange reaction exhibit a decreased bactericidal effect and their antimicrobial properties are not as long-lasting as is desired.

In the ion-exchange process, the antimicrobial metal ions tend to be converted into their oxides, hydroxides, basic salts, etc., either in the micropores or on the surfaces of the zeolite and also tend to deposit there, particularly when the concentration of metal ions in the vicinity of the zeolite surface is high. Such deposition can adversely affect the bactericidal properties of ion-exchanged zeolite.

In antimicrobial zeolite particles used in the present invention, ion-exchangeable ions present in zeolite, such as sodium ions, calcium ions, potassium ions and iron ions are partially replaced with ammonium and antimicrobial metal ions. Such ions may co-exist in the antimicrobial zeolite particle since they do not hinder the bactericidal effect. Antimicrobial metal ions other than silver can be ion-exchanged in the zeolite in addition to silver, so long as they do not impart antimicrobial action to the solution in the container. Other antimicrobial metal ions include ions of copper, zinc, mercury, tin, lead, bismuth, cadmium, chromium and thallium. Non-toxic antibiotic ions include gold, copper, and zinc ions.

The antimicrobial particles are preferably present in a concentration by weight in a container of the invention from about 0.5 to 5%, more preferably from about 0.5 to 3%, and most preferably from about 1 to 3%. The concentration will vary depending on the amount of silver in the zeolite. The antimicrobial metal ion is preferably present in the range

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of from about 0.1 to 5 wt. % of the zeolite.

A preferred antimicrobial zeolite for use in a contact lens case or container is Type A zeolite containing either a combination of ion-exchanged silver, zinc, and ammonium or silver and ammonium. One such zeolite is manufactured by Shinagawa, Inc. under the product number AW-10N and consists of 0.6% by weight of silver ion-exchanged in Type A zeolite particles having a diameter of about 2.5 $\mu$ . Another formulation, AJ-10N, consists of about 2% by weight silver ion-exchanged in Type A zeolite particles having a diameter of about 2.5 $\mu$ . Another formulation, AW-80, contains 0.6% by weight of silver ion-exchanged in Type A zeolite particles having a diameter of about 1.0 $\mu$ . Another formulation, AJ-80N, consists of about 2% by weight silver ion-exchanged in Type A zeolite particles having a diameter of about 1.0 $\mu$ . These zeolites contain from about 0.5% to 14% by weight of ion-exchanged ammonium. The zeolites are often obtained in master batches of low density polyethylene, polypropylene, or polystyrene, containing 20 wt.% of the zeolite.

The antimicrobial properties of the aqueous formulations of antimicrobial zeolite particles of the invention may be assayed using conventional assay techniques, including for example determining the minimum growth inhibitory concentration (MIC) with respect to a variety of bacteria, eumycetes, yeast, and other microbes. The MIC of antimicrobial agent is used to evaluate the efficacy of the agent *in vitro*. It is defined as the minimum concentration in micrograms/ml of antimicrobial agent required for inhibiting the growth of each type of microorganism. The smaller the MIC value, the greater the efficacy of the antimicrobial agent. The assay for determining MIC is known, and can be carried out by smearing a solution containing a particular microorganism for inoculation onto a plate culture medium to which a test sample of antimicrobial compound of the invention is added in a particular concentration, followed by incubation and culturing of the plate. In such a test, the microorganisms listed below, for example, may be employed: Streptococcus mutans, porphyromonas gingivalis, Bacillus cereus var mycoides, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus faecalis, Aspergillus niger, Aureobasidium pullulans, Chaetomium globosum, Gliocladium virens, Penicillium funiculosum, Candida albicans, and Saccharomyces cerevisiae.

Examples of contact lens cases of the invention are depicted in Figures 1-9. Figure 1 shows a contact lens container 1 of the invention comprising a polymeric material which is molded according to conventional techniques. The lens container 1 includes a

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bottom wall 2, a sidewall 3, and a sealable cap 4. The top of sidewall 3 may also include a threaded outer surface. Figure 3 further depicts the contact lens container of Figure 1, showing sealable cap 4 having a basket for holding one or more contact lenses, which basket is attached to the sealable cap by a stem 6 extending from an inner surface of cap 4. Figures 2, 3 and 5 show antimicrobial zeolite particles 7 and 13, either dispersed (7) throughout the polymeric material comprising lens container 1 (Figures 2 and 3), or deposited (13) on surfaces of the contact lens container 1 which contact a solution 8 used in the container.

The forms of solution dispensing container as well as methods for their production, are well known in the art. For example, a solution dispensing container 31 shown in Figure 10 comprises a molded substantially cylindrical shell having a bottom 32, a sidewall 35, a nozzle 33, and a sealable cap 34 at its top. The top of sidewall 35 may also include a threaded outer surface 36. Figures 11 and 12 show antimicrobial zeolite particles 7 and 13, either dispersed (7) throughout the polymeric material comprising solution bottle 31 (Figure 11), or deposited (13) on surfaces of the solution bottle 2 which contact solution.

The plastic resin is preferably a thermoplastic or thermosetting resin suitable for molding, such as injection molding or blow molding. Additionally, the resin is selected such that it is compatible with the antibiotic zeolite. One suitable class of resins is thermoplastic polyolefin resins, including high and low density polyethylene and polypropylene. Other suitable resins include polycarbonates, polyvinyl chlorides, polystyrene, such as acrylonitrile butadiene styrene, as well as other plastic resins known in the art.

Antimicrobial zeolite is incorporated in the resin by known methods. In one embodiment, the antimicrobial zeolite is provided in particulate form and the resin provided as polymer chips, which are blended together. Subsequently, the final blended material can be molded into an article by conventional molding methods, such as injection molding or blow molding. Alternatively, the article can be coated with one or more binders known generally in the art, such as acrylics, silicone adhesives, and hydrophilic polymers, which have the antimicrobial zeolite added thereto.

If desired, an antimicrobial contact lens case or container of the invention can be prepared by the process of applying, *e.g.*, direct spray coating, of an antimicrobial zeolite coating solution onto the lens case. The concentration of antimicrobial zeolite used in the coating solution is between 0.01 and 20%, preferably between 0.02 and 10%, and most

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preferably between 0.05 and 5%. The coating can be applied to the surfaces in contact with ophthalmic solution or to the entire case.

The coating material includes polymers, *e.g.*, silicone rubber, polyurethane, latex rubber, acrylic, PVC, or other polymer that can be coated to the surface of a container of the invention.

Alternatively, an antimicrobial container of the invention can be prepared by the process of dip coating, which comprises steps similar to that described for direct spray coating, *supra*, except that the coating is applied by dipping the contact lens case into the coating solution.

Another means for preparing an antimicrobial contact lens container of the invention comprises spray coating antimicrobial zeolite onto the external surface of the injection mold insert 14 as depicted in Figures 4 and 8. This is accomplished by incorporating antimicrobial zeolite into a binder and carrier that is compatible with the polymer being used, and applying the composition to the external surface of the mold insert, which methods are known generally in the art. Upon injection molding, the case or container will contain the antimicrobial component on its surface.

In addition to using antimicrobial zeolite directly with a binder, the zeolite can be incorporated into a solid polymer powder that is ground or atomized to a fine powder with a size from 5 to 800 microns, preferably 10 to 500 microns, and most preferably 50 to 300 microns. The powder contains 0.01 to 50% inorganic antimicrobial zeolite, preferably 0.05 to 30%, most preferably 1 to 20%. The powder is sprayed onto the mold with a carrier. During the injection molding process, the powder is incorporated into the surface of the polymer resulting in a container having an antimicrobial surface.

The following Examples are provided to further illustrate the antimicrobial contact lens case and container of the invention, and is not intended to provide limitations on any embodiment claimed.

#### EXAMPLE 1

##### *Preparation of a Contact Lens Case Containing Antimicrobial Zeolite*

Zeolite, prepared as described in U.S. Patent No. 4,938,955 issued to Niira et al., was combined with stearate (*e.g.*, Mg, Ca, Zn) in an amount equivalent to 5% wt. stearate of the zeolite. The stearate-zeolite mixture was added so that the amount of zeolite resulted

in 20% wt. of the polypropylene master batch, and compounded using a single or twin screw compounder. The mixture was poured into molds and allowed to set.

## EXAMPLE 2

### 5 Antimicrobial Efficacy of Contact Lens Case: Direct Inoculation Test

To demonstrate the antibacterial efficacy of the contact lens case prepared in Example 1, circular polypropylene test pieces (2.5 cm diameter) containing no zeolite (sample no. 1) or containing AW10D 2.0 % antimicrobial zeolite (sample no. 2) were washed with a neutral detergent, disinfected with a 70 % ethanol solution, and dried in an ultraviolet  
10 lamp box. Samples were then transferred to a gamma ray-sterilized polystyrene petri dish.

Since the samples were circular pieces, dripping of the inoculum suspension was modified as follows: 0.1 ml of the bacterial suspension (*S. aureus* or *E. coli* adjusted in a 1/4 Ringer solution), was dripped onto a uv-sterilized film (45x45 mm) and, using sterilized forceps, the test piece was carefully set over the suspension. This allowed complete contact  
15 between the suspension and the sample, thus avoiding undesired dehydration.

To check the physiological state of the test bacteria, 0.1 ml of the inoculum suspension was dripped directly into a "stomacker bag type 10" (control). Incubation of the inoculated sample and control were carried out at 35°C for 24 hours at ≥90% relative humidity.

20 Determination of viable bacteria after 24 hours incubation was made by the pour plate method using standard methods agar (35°C/48 hours). The following table illustrates the test results.

Sample	<i>S. aureus</i>	<i>E. coli</i>
1	$3.5 \times 10^4$	$1.7 \times 10^4$
2	Less than 10	Less than 10
Control	$8.8 \times 10^4$	$5.8 \times 10^6$
Inoculum	$2.8 \times 10^5$	$2.3 \times 10^5$

30 The table shows that the antimicrobial contact lens cases and containers of the invention impart substantial antimicrobial activity. Sample no. 2 which contained the zeolite

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composition of the invention had no bacterial growth, while sample no. 1 supported growth of both *S. aureus* and *E. coli*.

### EXAMPLE 3

#### 5     *Test for Leaching of Antimicrobial Zeolite*

A surprising advantage of the contact lens cases and containers of the invention is that antimicrobial component does not leach from the article into an ophthalmic solution in contact therewith. To demonstrate this property, an antimicrobial contact lens case of the invention was placed in contact with saline solution and the amount of silver ions  
10     that leached into the solution was quantified over a 6.5 hour period. Silver ions were detected using an ion selective electrode (ISE), and measurements were taken every two minutes. The graph in figure 13 charts the concentration of silver released into solution over time.

Minimal amounts of antimicrobial silver (at the sensitivity limit of the ISE) was leached into saline solution in contact therewith (*i.e.*, not enough to impart antimicrobial  
15     properties to the solution). After 6.5 hours the ISE reading was about 70 mV which was equivalent to about  $1.2 \times 10^{-11}$  ppm of silver in the solution. The flat line on the graph indicates that the concentration of silver ions did not change from the time that the solution was initially tested. Thus, a container of the invention for use with contact lenses and care products provides substantial antimicrobial protection (see Example 2) without leaching  
20     antimicrobial silver ions into the solution in contact therewith.



WHAT IS CLAIMED IS:

- 1                   1.     A contact lens container having a cavity adapted for holding one or  
2     more contact lenses and an ophthalmic solution therein, wherein the container comprises a  
3     polymeric material which contains antimicrobial zeolite comprising ion-exchanged silver in a  
4     concentration of between about 0.1 and 5 wt % of said zeolite, and ammonium ions in a  
5     concentration of between about 0.5 and 15 wt % of said zeolite, wherein the container does  
6     not leach said silver ions from the polymeric material into the ophthalmic solution in a  
7     substantially antimicrobial amount.
- 1                   2.     The contact lens container of claim 1 wherein said case has the  
2     property that it does not leach silver into an aqueous solution filling said container in an  
3     amount greater than 100 ppb following twenty-four hour exposure.
- 1                   3.     The contact lens container of claim 1 wherein polymeric material is  
2     selected from polypropylene, polyethylene, low density polypropylene, high density  
3     polypropylene, acrylonitrile butadiene styrene, and polystyrene.
- 1                   4.     The contact lens container of claim 1 wherein the amount of silver is  
2     between about 1 to 3 wt % of the zeolite.
- 1                   5.     The contact lens container of claim 1 wherein the zeolite is between  
2     about 0.5 and 5 wt. % of the polymeric material and is dispersed therein.
- 1                   6.     The contact lens container of claim 1 wherein the container has a  
2     surface coating comprising the polymeric material in a powdered form and the zeolite.
- 1                   7.     A container for dispensing a contact lens solution, having an internal  
2     surface which contacts a solution, an external surface, a dispensing means at one end of the  
3     container for dispensing the solution, and a means for sealing the container at the dispensing  
4     means, wherein the container comprises antimicrobial polymeric material which contains a  
5     zeolite comprising ion-exchanged silver in a concentration of between about 0.1 and 5 wt %

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1 of said zeolite, and ammonium ions in a concentration of between about 0.5 and 15 wt % of  
2 said zeolite, wherein the container does not leach said silver ions from the polymeric material  
3 into the ophthalmic solution in a substantially antimicrobial amount.

1 8. The container of claim 3 wherein said container has the property that it  
2 does not leach silver into an aqueous solution filling said container in an amount greater than  
3 100 ppb following twenty-four hour exposure.

1 9. The container for dispensing a contact lens solution of claim 3 wherein  
2 the polymeric material is selected from polypropylene, polyethylene, low density  
3 polypropylene, high density polypropylene, acrylonitrile butadiene styrene, and polystyrene.

1 10. The contact lens container of claim 4 wherein the amount of silver is  
2 between about 1 to 3 wt % of the zeolite.

1 11. The container for dispensing a contact lens solution of claim 3 wherein  
2 the zeolite is between about 0.5 and 5 wt. % of the polymeric material and is dispersed  
3 therein.

1 12. The container for dispensing a contact lens solution of claim 3 wherein  
2 the container has a surface coating comprising the polymeric material in a powdered form and  
3 the zeolite.

1 13. The contact lens container of claim 1 made by the process of molding  
2 the polymeric material which comprises the zeolite dispersed within the polymeric material  
3 in an amount between about 0.5 and 5 wt. % of the polymeric material.

1 14. The contact lens container of claim 1, wherein the container has a  
2 surface coating containing the zeolite, made by the process of applying the zeolite onto a  
3 mold for forming the container, and adding the polymeric material to the mold, to form the  
4 contact lens container of claim 1.

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1                   15.    The contact lens container of claim 1, wherein the container has a  
2   surface coating containing the zeolite, made by the process of applying the zeolite to the  
3   container.

1                   16.    The container for dispensing a contact lens solution of claim 7 made by  
2   the process of molding the polymeric material which comprises zeolite dispersed within the  
3   polymeric material in an amount between about 0.5 and 5 wt. % of the polymeric material.

1                   17.    The container for dispensing a contact lens solution of claim 7,  
2   wherein the container has a surface coating containing the zeolite, made by the process of  
3   applying the zeolite onto a mold for forming the container, and adding the polymeric  
4   material to the mold, to form the container of claim 7.

1                   18.    The contact lens container of claim 7, wherein the container has a  
2   surface coating containing the zeolite, made by the process of applying the zeolite directly  
3   onto the surface of the container, dispensing means, and means for sealing the container.

1                   19.    A method for inhibiting or retarding the growth of microbes on a  
2   contact lens during periods when the lens is not used in the eye, which comprises storing a  
3   contact lens in the container of claim 1.

1                   20.    A method for inhibiting or retarding the growth of microbes in a  
2   solution which comprises storing the solution in a container of claim 7.

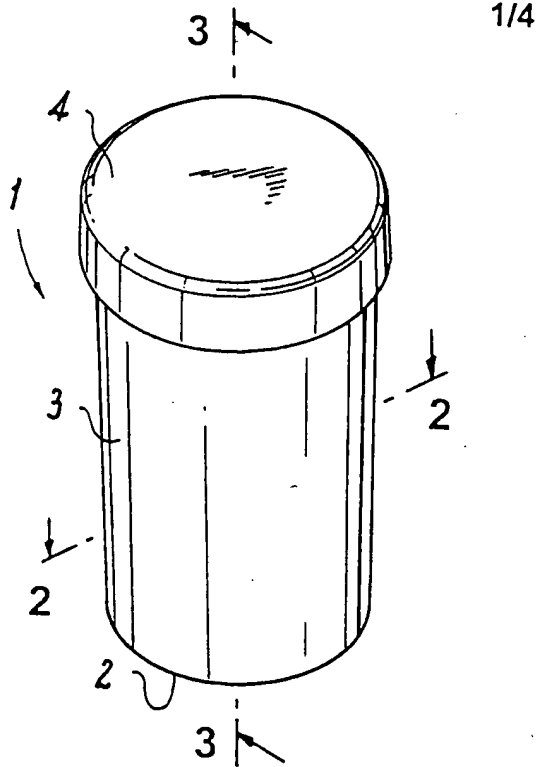


FIG. 1

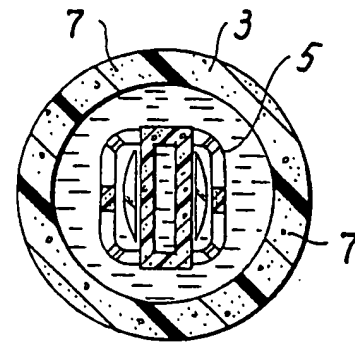


FIG. 2

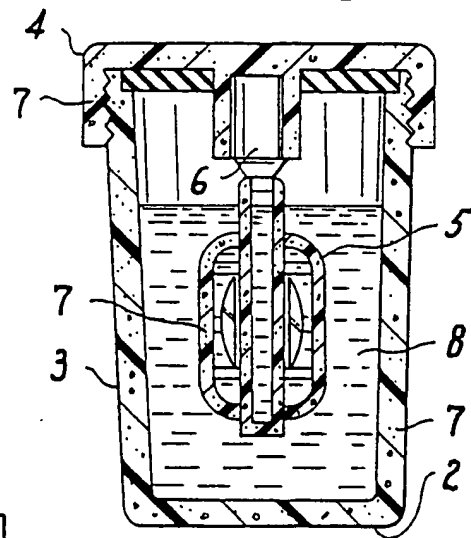


FIG. 3

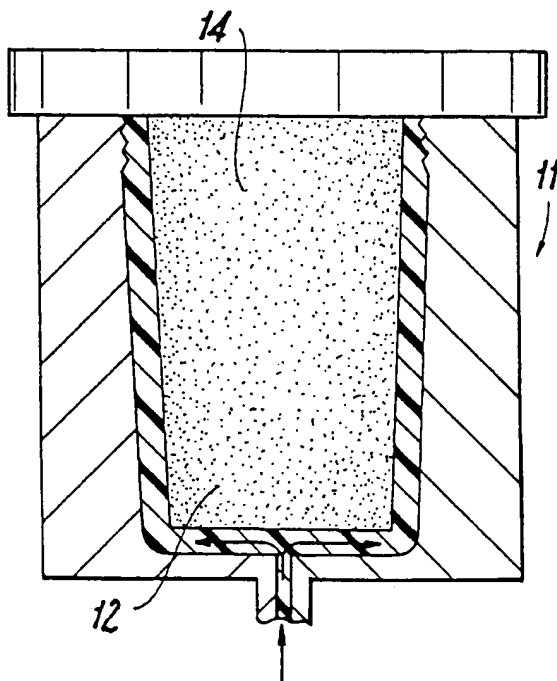


FIG. 4

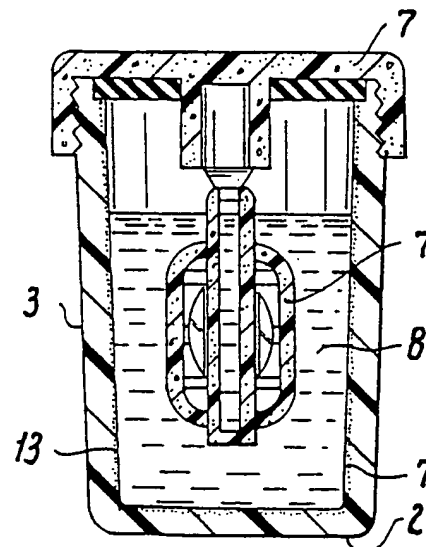


FIG. 5

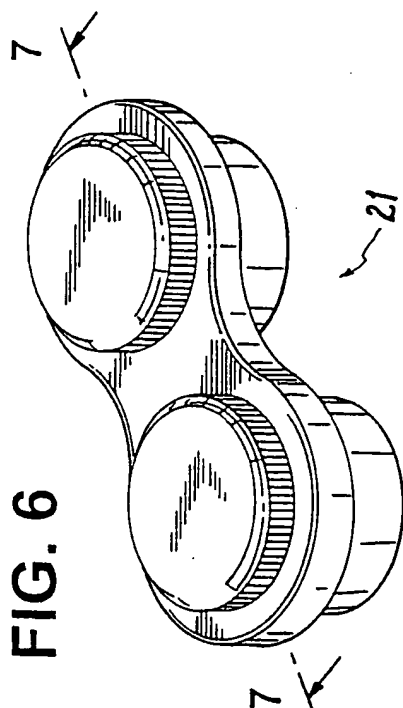


FIG. 6

FIG. 7

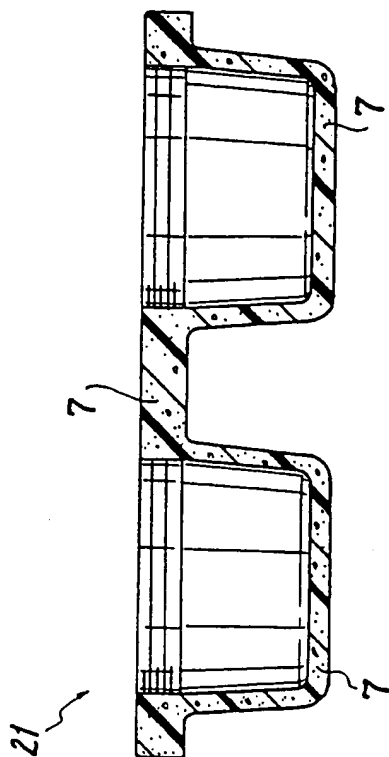
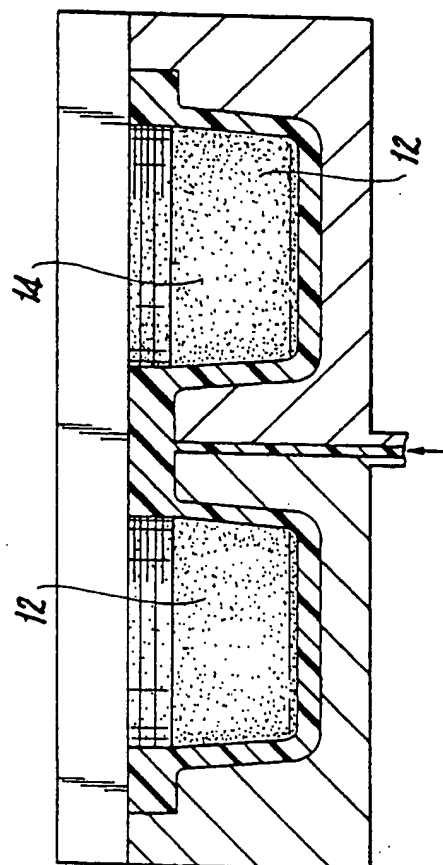


FIG. 8

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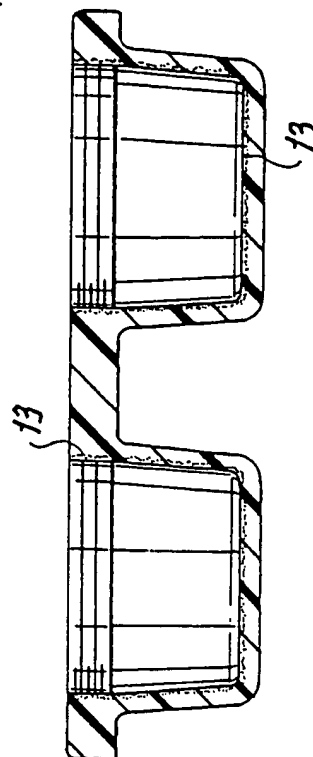


FIG. 9

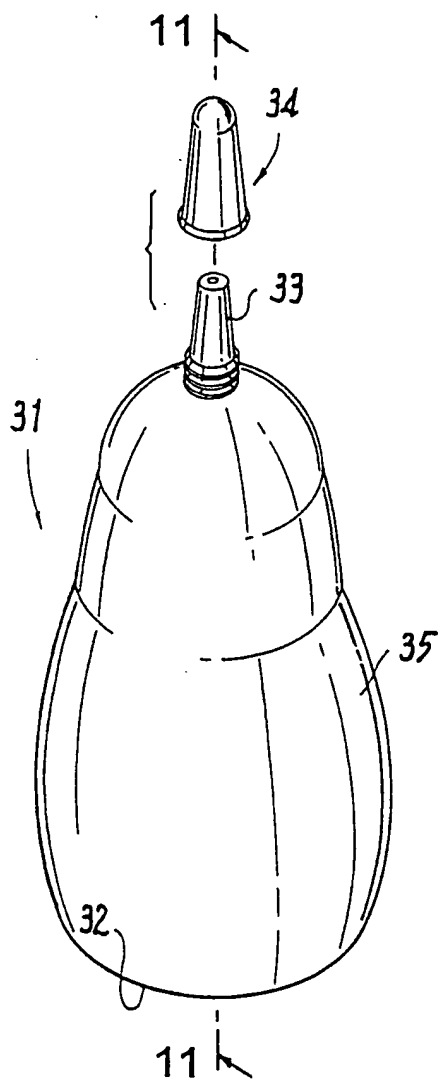


FIG. 10

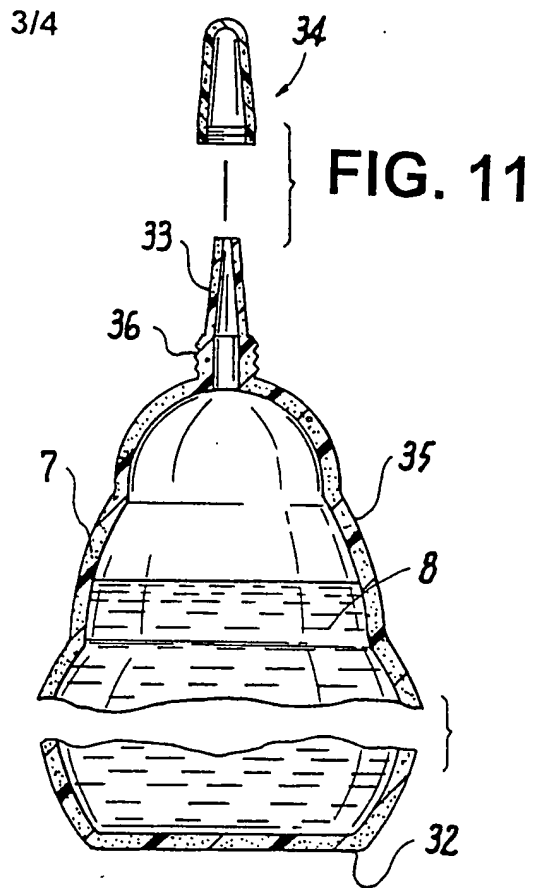


FIG. 11

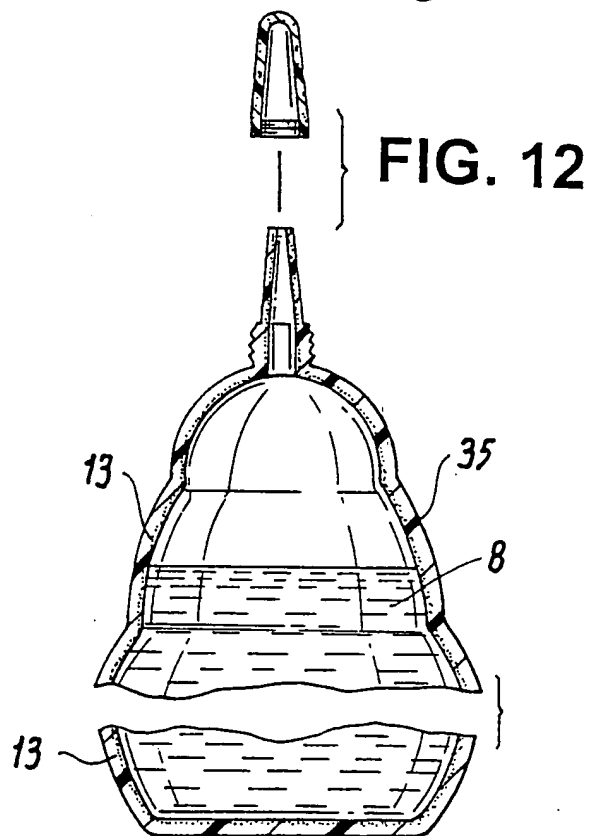
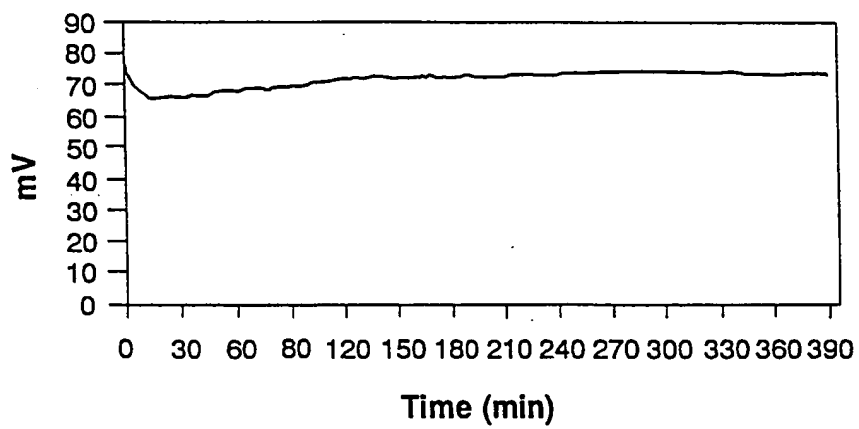


FIG. 12

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**Polypropylene for Lens Case****FIG. 13**

# INTERNATIONAL SEARCH REPORT

b. National Application No

PCT/US 99/31027

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 A45C11/00 C08K9/02

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A45C C08K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

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X	EP 0 640 661 A (SHINETSU CHEMICAL CO) 1 March 1995 (1995-03-01) page 4, line 45 - line 48 page 5; table 1 page 5; examples 1-5 claims 1-6	1-20
A	US 5 340 583 A (DZIABO ANTHONY J ET AL) 23 August 1994 (1994-08-23) claims 1-13	1-20

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

30 March 2000

Date of mailing of the international search report

06/04/2000

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Information on patent family members

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